Correspondence

Science Funding

(*Editor's Note: Following is a reprint of a letter sent to Donna Shalala, secretary of the Department of Health and Human Services, on 9 June 1995.*)

The budget now under consideration in the Congress for the National Institute of Environmental Health Sciences would indefensibly threaten environmental health protection for America. For millions of Americans the environment is a major determinant of their health, and for the quarter-century that it has existed, the National Institute of Environmental Health Sciences has been the first line of defense against these threats. Its record of success is unsurpassed among the National Institutes of Health. Now, as an increasing number of disorders ranging from premature births to a wide variety of cancers, appear to have an environmental cause or component, a fully funded NIEHS is essential.

NIEHS is unique among the institutes. By focusing its research efforts on the health impacts of environmental exposures, ranging from air pollution to food additives, NIEHS provides cross-cutting support to the other institutes and a wide range of regulatory agencies. There is no question that NIEHS-supported research has improved the quality of life in response to a deep and abiding commitment by the public to environmental protection. Moreover, NIEHS programs have been instrumental in making the United States the world's leader in biomedical research, providing a foundation for the nation's expanding, highly profitable biotechnology industry. One of the more prominent NIEHS researchers is a Nobel laureate, and most are world leaders in their field of inquiry.

NIEHS-sponsored research is opening the door to an understanding of the molecular and cellular-level mechanisms by which diseases and disorders are caused, making it possible to develop methods of prevention and treatment for all illnesses, not just those with environmental causes. For example, within the last year alone, NIEHS researchers have discovered the gene that causes breast cancer and another that is associated with metastasis of cancer of the prostate.

What's Your Perspective?

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Most importantly, literally every American, especially our children and elderly, is today safer and healthier because of research supported by the National Institute of Environmental Health Sciences. Collectively, this reduction in the nation's burden of illness due to environmental exposures has been cost effective by virtually any measure. Consider, for example, that:

- NIEHS research on the effects of lead on children's nervous systems caused it to be removed from gasoline, safeguarding the intelligence of American children. Other research associating lead with elevated blood pressure, and therefore increased risk of heart attack and stroke in men, was instrumental in eliminating this ubiquitous metal from a variety of other uses, ranging from plumbing solder to paints.
- NIEHS studies of pesticides—aldrin, dieldrin, and heptachlor, to name but three—helped demonstrate the dangers of pesticides generally, supporting regulations that have made food safer for consumers and work less threatening for farm families.
- Research on air pollutants such as ozone, sulfur dioxide, and carbon monoxide demonstrating, for example, that particulate pollution is associated with roughly 60,000 deaths per year, has laid the groundwork for the national effort to lower the levels of these compounds. There can be little doubt that tens of millions of Americans are healthier because of these efforts. Others are, quite literally, alive because of them.

Due to its expertise, NIEHS has been assigned responsibility for programs funded through other laws. For example, the institute has provided health and safety training and education to more than 100,000 workers involved in the cleanup of hazardous waste sites or responses to toxic chemical releases.

The list of NIEHS successes could continue for pages, but despite these achievements much remains to be done. Environmental agents, including not only air and water pollutants, but food contaminants, tobacco smoke, and workplace chemicals, are implicated as a cause or component in a wide range of diseases.These include cancers of the brain, breast, pancreas, prostate, testicle, and a variety of other organs. Some serious diseases in which environmental exposures are implicated are increasing at an alarming rate. These include, for example, asthma, especially in children. Environmental causes have been implicated in all these, as well as Alzheimer and Parkinson diseases, premature births, spontaneous abortions, liver and kidney disorders, as well as a wide range of other illnesses.

The proposed budget threatens both current and future research at a time when both the Congress and the administration will require more and better information because of legislation designed to compel the application of science through risk assessments and cost–benefit analysis. Adopting that budget will cripple the effort to assure that sound science underlies national regulatory decisions. It also will require drastic, immediate revisions that will threaten the nation's ability to maintain a viable biomedical research establishment which, in turn, will reduce our ability to cure disease and, especially, prevent it.

We urge you to share our views with Members of Congress and to spare no effort to assure that the National Institute of Environmental Health Sciences is funded at least to the level propsed by the president. Further, we urge you and your colleagues in the administration to speak out, and vigorously defend not only the budget of the National Institute of Environmental Health Sciences, but those of the other institutes as well.

The National Advisory Environmental Health Sciences Council

Norma C. Barfield
Ann Arbor, Michigan

Patricia A. Buffler
University of California
Berkeley, California

Doyle G. Graham
Duke University Medical Center
Durham, North Carolina

Bernadette Gray-Little
University of North Carolina
Chapel Hill, North Carolina

Phylis Greenberger
The Society for the Advancement of Women's Health Research
Washington, DC

Philip S. Guzelian
University of Colorado
Health Sciences Center
Denver, Colorado

Maureen Henderson
Fred Hutchinson Cancer Research Center
Seattle, Washington

Rogene Henderson
Lovelace Inhalation Toxicology Research Institute
Albuquerque, New Mexico

Lovell Jones
The University of Texas
Houston, Texas

Michael Lieberman
Baylor College of Medicine
Houston, Texas

Curtis A. Moore
McLean, Virginia

Rafael Moure
University of Lowell
Lowell, Massachusetts

Thomas E. Norris
School of Medicine
University of North Dakota
Grand Forks, North Dakota

Cecil B. Pikett
Schering Plough Research Institute
Kenilworth, New Jersey

Macolm C. Pike
University of Southern California
Los Angeles, California

George Provenzano
University of Maryland
Baltimore, Maryland

Donald J. Reed
Orgeon State University
Corvallis, Oregon

Mary Vore
College of Medicine
University of Kentucky
Lexington, Kentucky

I. Bernard Weinstein
Columbia-Presbyterian Cancer Center
New York, New York

Inflammation: More Than One Explanation

I read with interest the *EHP* supplement on oxygen radicals and lung injury (vol. 102, supplement 10). I would like to take this opportunity to comment about this supplement and raise a key issue concerning the major concepts regarding the mechanisms of cellular injury in inflammatory diseases.

As an active investigator in this field of research, I cannot fully understand why there was no mention in the supplement about the basic understanding that cellular damage in inflammation is multifactorial. The nonexpert reader of this supplement might receive an erroneous impression that oxygen radicals, per se, are the exclusive toxic agonists that induce cellular injury. Many in this field share the view that cellular damage in inflammatory diseases might be caused by a "coordinated cross-talk" among oxidants, membrane-damaging agents, proteinases, arachidonic acid metabolites, phospholipases, cationic proteins, and cytokines. All these agents are likely to be present in sites of infection and inflammation. But sadly, none of the publications elaborating on this multifactorial view are quoted in modern textbooks or in symposia on inflammation and inflammatory diseases. Instead, the literature is filled with publications that insist on a single agonist, be it an oxidant, a protease, a cytokine, etc., in experimental models. No attempt to integrate the various agonists into the full picture is made.

Several of our publications (*1–7*) deal with synergistic interactions among multiple proinflammatory agonists in cellular injury during inflammation. I believe that this issue is important, timely, and might contribute to an understanding of how drugs, chemicals, and xenobiotics function *in vivo*.

Isaac Ginsburg
Hadassah School of Dental Medicine
Hebrew University
Jerusalem

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Response

We appreciate the interest shown by Dr. Ginsburg in our recent conference proceedings (*EHP* 102, supplement 10). As stated in the preface of those proceedings, The Oxygen Radicals and Lung Injury Conference was the first of its kind dedicated to pulmonary science. Therefore, in this conference, the primary attempt was to focus on oxygen radicals and their involvement in toxic insults and the ensuing pathophysiological processes in the lung. We did not ignore the importance of multifactorial relationships of other cellular reactions and products involved in cellular damage and injury. In fact, these issues were addressed in the presentations of Ward (*1*), Holian et al. (*2*), Repine (*3*), Torphy et al. (*4*), and Demers and Kuhn (*5*). The complex network of micromolecular reactions have not been fully defined to understand the coordination, modulation, and integration of cellular functions. In many pulmonary diseases (e.g., cancer, emphysema, pneumoconiosis) in which oxygen radicals are implicated, the disease becomes evident only after several years. Subtle damage or changes to biomolecules and their relationships to the coordination and interactions of oxygen radical generation and degradation are important issues to be dealt with in greater detail to understand the synergistic concepts of lung dieases. We hope that future conferences will address these and other issues.

V. Vallythan
V. Castranova
K. Weber
National Institute of Occupational
Safety and Health
Morgantown, West Virginia

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MTBE: Not Carcinogenic

Subsequent to publication of *EHP*'s timely article on the toxicological potential of methyl-*tert*-butyl ether (MTBE; vol. 103, pp. 666–670), the long-awaited study from the Ramazzini Foundation of Oncology and Environmental Sciences appeared in print (*1*). This was a landmark publication because for months we in the scientific community had been advised that the data predicted dire health hazards for humans exposed